

WE CLAIM:

1. An isolated consensus DNA sequence of the BRCA1 coding sequence as set forth in SEQ. ID. NO.: 1.
2. A consensus protein sequence of the BRCA1 protein as set forth in SEQ. ID. NO.: 2.
3. An isolated coding sequence of the BRCA1 gene as set forth in SEQ. ID. NO.: 3.
4. A protein sequence of the BRCA1 protein as set forth in SEQ. ID. NO.: 4.
5. An isolated coding sequence of the BRCA1 gene as set forth in SEQ. ID. NO.: 5.
6. A protein sequence of the BRCA1 protein as set forth in SEQ. ID. NO.: 6.
7. A BRCA1 gene with a BRCA1 coding sequence not associated with breast or ovarian cancer which comprises an alternative pair of codons, AGC and AGT, which occur at position 2201 at frequencies of about 35-45%, and from about 55-65%, respectively.
8. A BRCA1 gene according to Claim 7 wherein AGC occurs at a frequency of about 40%.
9. A set of at least two alternative codon pairs which occur at polymorphic positions in a BRCA1 gene with a BRCA1 coding sequence not associated with breast or ovarian cancer, wherein codon pairs are selected from the group consisting of:
 - AGC and AGT at position 2201;
 - TTG and CTG at position 2430;

- CCG and CTG at position 2731;
- GAA and GGA at position 3232;
- AAA and AGA at position 3667;
- TCT and TCC at position 4427; and
- AGT and GGT at position 4956.

10. A set of at least two alternative codon pairs according to claim 9, wherein the codon pairs occur in the following frequencies, respectively, in a population of individuals free of disease:

- at position 2201, AGC and AGT occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 2430, TTG and CTG occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 2731, CCG and CTG occur at frequencies from about 25-35%, and from about 65-75%, respectively;
- at position 3232, GAA and GGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 3667, AAA and AGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 4427, TCT and TCC occur at frequencies from about 45-55%, and from about 45-55%, respectively; and
- at position 4956, AGT and GGT occur at frequencies from about 35-45%, and from about 55-65%, respectively.

11. A set according to Claim 10 which is at least three codon pairs.

12. A set according to Claim 10 which is at least four codon pairs.

13. A set according to Claim 10 which is at least five codon pairs.

14. A set according to Claim 10 which is at least six codon pairs.

15. A set according to Claim 10 which is at least seven codon pairs.

16. A method of identifying individuals having a BRCA1 gene with a BRCA1 coding sequence not associated with disease, comprising:

- (a) amplifying a DNA fragment of an individual's BRCA1 coding sequence using an oligonucleotide primer which specifically hybridizes to sequences within the gene;
- (b) sequencing said amplified DNA fragment by dideoxy sequencing;
- (c) repeating steps (a) and (b) until said individual's BRCA1 coding sequence is completely sequenced;
- (d) comparing the sequence of said amplified DNA fragment to a BRCA1^(oml) DNA sequence, SEQ. ID. NO1, SEQ. ID. NO3, or SEQ. ID. NO5;
- (e) determining the presence or absence of each of the following polymorphic variation in said individual's BRCA1 coding sequence:
 - AGC and AGT at position 2201,
 - TTG and CTG at position 2430,
 - CCG and CTG at position 2731,
 - GAA and GGA at position 3232,
 - AAA and AGA at position 3667,
 - TCT and TCC at position 4427; and
 - AGT and GGT at position 4956;
- (f) determining any sequence differences between said individual's BRCA1 coding sequences and SEQ. ID. NO1, SEQ. ID. NO3, or SEQ. ID. NO5 wherein the presence of said polymorphic variations and the absence of a variation outside of positions 2201, 2430, 2731, 3232, 3667, 4427, and 4956, is correlated with an absence of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA1 mutation in the BRCA1 coding sequence.

17. A method of claim 16 wherein, codon variations occur at the following frequencies, respectively, in a caucasian population of individuals free of disease:

- at position 2201, AGC and AGT occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 2430, TTG and CTG occur at frequencies from about 35-45%, and from about 55-65%, respectively;

- at position 2731, CCG and CTG occur at frequencies from about 25-35%, and from about 65-75%, respectively;
- at position 3232, GAA and GGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 3667, AAA and AGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 4427, TCT and TCC occur at frequencies from about 45-55%, and from about 45-55%, respectively; and
- at position 4956, AGT and GGT occur at frequencies from about 35-45%, and from about 55-65%, respectively.

18. A method according to claim 16 wherein said oligonucleotide primer is labeled with a radiolabel, a fluorescent label a bioluminescent label, a chemiluminescent label, or an enzyme label.

19. A method of detecting a increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA1 coding sequence, comprising:

- amplifying a DNA fragment of an individual's BRCA1 coding sequence using an oligonucleotide primer which specifically hybridizes to sequences within the gene;
- sequencing said amplified DNA fragment by dideoxy sequencing;
- repeating steps (a) and (b) until said individual's BRCA1 coding sequence is completely sequenced;
- comparing the sequence of said amplified DNA fragment to a BRCA1^(omi) DNA sequence, SEQ. ID. NO1, SEQ. ID. NO3, or SEQ. ID. NO5;
- determining any sequence differences between said individual's BRCA1 coding sequences and SEQ. ID. NO1, SEQ. ID. NO3, or SEQ. ID. NO5; to determine the presence or absence of base changes in said individual's BRCA1 coding sequence wherein a base change which is not any one of the following:
 - AGC and AGT at position 2201,
 - TTG and CTG at position 2430,
 - CCG and CTG at position 2731,

- GAA and GGA at position 3232.
- AAA and AGA at position 3667,
- TCT and TCC at position 4427, and
- AGT and GGT at position 4956 is correlated with the potential of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA1 mutation in the BRCA1 coding sequence.

20. A method of claim 19 wherein, codon variations occur at the following frequencies, respectively, in a population free of disease:

- at position 2201, AGC and AGT occur at frequencies from about 40%, and from about 55-65%, respectively;
- at position 2430, TTG and CTG occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 2731, CCG and CTG occur at frequencies from about 25-35%, and from about 65-75%, respectively;
- at position 3232, GAA and GGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 3667, AAA and AGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 4427, TCT and TCC occur at frequencies from about 45-55%, and from about 45-55%, respectively; and
- at position 4956, AGT and GGT occur at frequencies from about 35-45%, and from about 55-65%, respectively.

21. A method according to claim 19 wherein said oligonucleotide primer is labeled with a radiolabel, a fluorescent label a bioluminescent label, a chemiluminescent label, or an enzyme label.

22. A set of codon pairs, which occur at polymorphic positions in a BRCA1 gene with a BRCA1 coding sequence according to Claim 1, wherein said set of codon pairs is:

- AGC and AGT at position 2201;
- TTG and CTG at position 2430;
- CCG and CTG at position 2731;
- GAA and GGA at position 3232;

- AAA and AGA at position 3667;
- TCT and TCC at position 4427; and
- AGT and GGT at position 4956.

23. A set of at least two alternative codon pairs according to claim 22 wherein set of at least two alternative codon pairs occur at the following frequencies:

- at position 2201, AGC and AGT occur at frequencies of about 40%, and from about 55-65%, respectively;
- at position 2430, TTG and CTG occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 2731, CCG and CTG occur at frequencies from about 25-35%, and from about 65-75%, respectively;
- at position 3232, GAA and GGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 3667, AAA and AGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 4427, TCT and TCC occur at frequencies from about 45-55%, and from about 45-55%, respectively; and
- at position 4956, AGT and GGT occur at frequencies from about 35-45%, and from about 55-65%, respectively.

24. A BRCA1 coding sequence according to claim 1 wherein the codon pairs occur at the following frequencies:

- at position 2201, AGC and AGT occur at frequencies of about 40%, and from about 55-65%, respectively;
- at position 2430, TTG and CTG occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 2731, CCG and CTG occur at frequencies from about 25-35%, and from about 65-75%, respectively;
- at position 3232, GAA and GGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 3667, AAA and AGA occur at frequencies from about 35-45%, and from about 55-65%, respectively;
- at position 4427, TCT and TCC occur at frequencies from about 45-55%, and from

- about 45-55%, respectively; and
- at position 4956, AGT and GGT occur at frequencies from about 35-45%, and from about 55-65%, respectively.
25. A method of determining the consensus genomic sequence or consensus coding sequence for a target gene, comprising:
- a) screening a number of individuals in a population for a family history which indicates inheritance of normal alleles for a target gene;
 - b) isolating at least one allele of the target gene from individuals found to have a family history which indicates inheritance of normal alleles for a target gene;
 - c) sequencing each allele;
 - d) comparing the nucleic acid sequence of the genomic sequence or of the coding sequence of each allele of the target gene to determine similarities and differences in the nucleic acid sequence; and
 - e) determining which allele of the target gene occurs with the greatest frequency.
26. A method of performing gene therapy, comprising:
- a) transfecting cancer cell *in vivo* with an effective amount of a vector transformed with a BRCA1 coding sequences of SEQ. ID. NO.: 1, SEQ. ID. NO.: 3, or SEQ. ID. NO.: 5;
 - b) allowing the cells to take up the vector, and
 - c) measuring a reduction in tumor growth.
27. A method of performing protein therapy, comprising:
- a) injecting into a patient, an effective amount of BRCA1 tumor growth inhibiting protein of SEQ. ID. NO.: 2, SEQ. ID. NO.: 4, or SEQ. ID. NO.: 6;
 - b) allowing the cells to take up the protein, and
 - c) measuring a reduction in tumor growth.

Add (B)